3D metabolic ex vivo sample imaging of hyperpolarized compounds using a 3D single-shot RARE (3D SS-RARE) sequence, combining spectral RF selectivity with under-sampled spectral encoding at signal read-out

Magnusson, P.O.; Jensen, Pernille Rose; Dyrby, T. B.; Karlsson, Magnus; Lerche, Mathilde Hauge; Hanson, Lars G.

Published in:
Proceedings of 5th hyperpolarization symposium

Publication date:
2015

Document Version
Peer reviewed version

3D Metabolic ex vivo sample imaging of hyperpolarized compounds using a 3D Single-Shot RARE (3D SS-RARE) sequence, combining spectral RF selectivity with under-sampled spectral encoding at signal read-out

P.O. Magnusson[1], P.R. Jensen[3], T.B. Dyrby[1], M. Karlsson[3], M.H. Lerche[3] and L.G. Hanson[1,2]

[1]Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark [2]DTU Elektro, Technical University of Denmark, Lyngby, Denmark [3]Albeda Research Aps, Valby, Denmark

Introduction: Magnetic Resonance Spectroscopy (MRS) of Hyperpolarized (HP) metabolically active 13C-enriched compounds has been shown to be a powerful method for in vivo cancer diagnosis[1]. Histology of sentinel lymph node ex vivo tissue samples is used in clinical routine for diagnosis of breast cancer metastasis[2]. This histological procedure requires time consuming sample analysis. 3D hyperpolarized MRS-imaging (MRSI) can potentially speed up the diagnosis of metastasis in excised lymph nodes if enough hyperpolarized sample can be injected into the tissue ex vivo and if it can be sufficiently distributed. We have therefore designed and optimized a 3D MRSI pulse sequence for this purpose.

Theory: Since the entire imaged sample can be confined within the image volume, 3D MR imaging of ex vivo samples allows for complete spatial non-selectivity of RF pulses, and chemical shift localization errors does not need to be considered in the selection of RF pulses. For the ex vivo sample application, only the product signals are of interest and frequency selective excitation is thereby necessary. With limited number of signals, under-sampled spectral encoding at signal read-out in combination with the high SNR characteristics of the fast spin-echo sequence (RARE) becomes an attractive alternative, given that a long enough apparent T2 relaxation time (aT2) can be ensured.

Methods: 3D SS-RARE was implemented on an 4.7T pre-clinical MR-scanner (Agilent Inc., USA) with a gradient-echo train (GET) applied during spin-echo formation. The excitation was frequency selective over 740Hz and the refocusing selected to ensure inversion of substrate magnetization outside the excitation pass-band. The phase-encoding employed cartesian spiral order with elliptical truncation. The sequence were tested on a thermal multi-compartment phantom and on a HP single resonance compound (HP001) injected into a lymph node with a ceramic needle. A volume transmit and a loop surface receive coil (Rapid Biomedical GmbH, Rimpar, Germany) were used with the phantom and lymph node centred in the loop coil. Substrates were polarised and dissolved with a HyperSense polariser (Oxford instruments). Phantom scan parameters: FOV=40x40x40mm^3, matrix=32x16x16, ETL=208(ph.encodings), ESP=25ms, GET-length=17, GET-ESP=1.028ms, scan time=5.2s. Lymp node scan parameters: FOV=48x18x18mm^3, matrix=32x12x12, ETL=112, ESP=26ms, GET-length=17, GET-ESP=1.208ms, scan time=2.9s. aT2 was determined for 1-13C-Acetate, 1-13C-Pyruvate, and for HP001 in lymph node.

Results and Discussion: The measured aT2-values in lymph node for 1-13C-Acetate (aT2=3.4s), 1-13C-Pyruvate (aT2=1.4s) and HP001 (aT2=2.8s) were long enough for efficient utilization of the magnetization with 3D SS-RARE. With the optimized protocol and for the phantom experiment, the 3D SS-RARE was able to separate two components with the under-sampled spectral encoding while excluding two other components outside the excitation pass-band (**Figure 1A**). 3D SS-RARE 13C-images of HP001 injected into the lymph node was acquired with a isotropic resolution of 1.5x1.5x1.5mm^3 giving an SNRmax=542 (**Figure 1B**). The spatial 13C-signal distribution over the lymph node was characterized by a sub-region of max signal and with varying signal decay away from this point along different directions over the lymph node. This suggests that the max signal sub-region corresponds to the location of the injection and that the injected substance is distributed in the tissue surrounding. This indicates that the selected injection technique is feasible. Further insight into the tissue sample 13C spatial signal distribution can be obtained if 3D SS-RARE is used with higher resolution, which should be possible given the high SNR obtained in this experiment.

Conclusion: A 3D SS-RARE sequence was implemented, optimized and experimentally tested for metabolic imaging of hyperpolarized substances injected into lymph node tissue samples, with the end goal of metastasis detection. Desired spectral separation could be achieved on phantoms and lymph node images could be acquired with SNR=524 for a spatial resolution of 1.5x1.5x1.5mm^3, which shows the great potential of the 3D SS-RARE sequence in this context.

References: [1] Golman et al., PNAS 103: 11270 (2006), [2] Diest et al., Breast Disease 31:65-81 (2010).

Acknowledgements: This work was sponsored by the Innovation Fund, Denmark (19-2013-3).

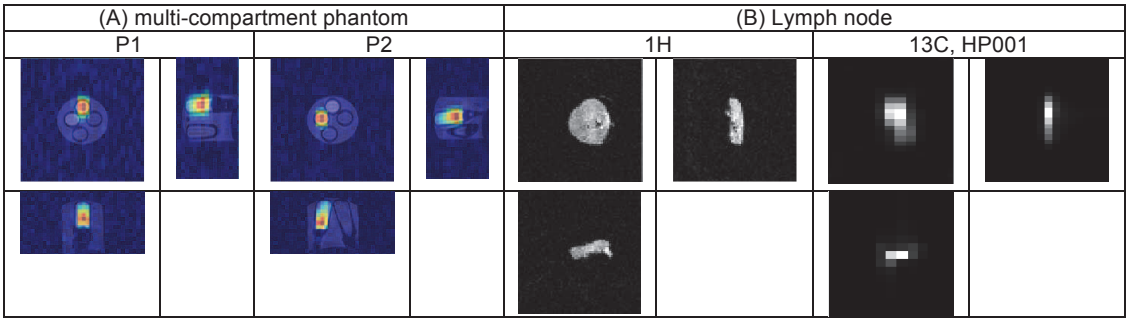

Figure 1. (A) Separation with the 3D SS-RARE sequence of the two components P1 (3M) and P2 (4M), 320Hz apart in a multi-compartment phantom. The two other components are outside the RF excitation pass-band. 13C-images are displayed as color-coded overlays on corresponding 1H-images. (B) Images acquired with 3D SS-RARE of single resonance hyperpolarized HP001 injected into a lymph node. 13C-images were spatially scaled to the 1H-images using nearest-neighbour interpolation.